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08/817,595

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/817,595	04/22/97	TURTAUD	A MANG1-15

EXAMINER

H421/102

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ART UNIT	PAPER NUMBER
1642	12

DATE MAILED: 10/27/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 8-11-98

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-24 is/are pending in the application.
Of the above, claim(s) 1-9 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 10-24 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☑ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☑ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☑ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2 sheets
☐ Interview Summary, PTO-413
☒ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. Applicant's amendment filed August 19, 1998 (Paper No: 11/B) is acknowledged. Accordingly, claims 10-16 are amended, claims 1-9 are cancelled and claims 17-24 are added.

Claims 10-24 are being examined.

2. The amendments to the specification have been noted, reviewed and entered.

Response to Arguments

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The objections to the specification in paragraph 1 of the previous office action (mailed 3/31/98) is withdrawn in view of amendments.

5. The following rejections are withdrawn in view of amendment to the claims:

A. Rejection of claims 10-16 (moot with respect to cancelled claims 1-9) under 35 U.S.C.112, second paragraph in view of amendments and explanations.

B. Rejection of claims 1-7 under 35 U.S.C.112, first paragraph are moot as claims are cancelled.

C. Rejection of claim 10 (moot with respect to cancelled claims 1-3, 8-9) under 35 U.S.C.102(b) is withdrawn in view of amendments to the claims.

6. Rejection of claim under 35 U.S.C.103(a) is withdrawn in view of the amendments to the claims. Th references of Stott et al was relevant to the rejection as set forth for the claims prior to amendments. Applicant amended the claims to refer to treatment of cancer, whereas the original claim was drawn also to generation of an immune response. However, this rejection (as well as

the reference of Stott et al) is being withdrawn as the claims are now drawn to cancer therapy. As is elaborated below, the amended claims now raise issues of enablement of the invention.

New Grounds of Rejection

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 10-13, 17- 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims are ambiguous in that they are drawn to a composition comprising at least to containers useful for the treatment of cancers. Clarification is requested.

B. Claims are indefinite in that the differences between the two sources of animal tissue , serum or cells in the two containers are not clear. Are the differences in the sources from different tissues or cells (e.g. muscle vs brain and T cells vs epithelial cells) or due to different batches of the same ? or different species or different members of the same species? Clarification is requested.

C. Claims are indefinite in the recitation of "effective amount" as the metes and bounds are not clear.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 17-22, 10-13, 14-16, 23-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims are drawn to a pharmaceutical composition useful for the treatment of cancer comprising MHC molecules, and methods of preparing the pharmaceutical composition, and a method of treating cancers. In determining the enablement of the instant claims, some of the factors that were considered were 1) nature of the invention, b) state of the prior art, c) level of predictability, d) amount of direction given, e) existence of working examples, f) quantity of experimentation to make the invention. The nature of the invention is such that the pharmaceutical composition of the instant claims must have a therapeutic benefit and b able to treat cancer. Treatment of cancer is recognized to mean treatment of the disease with its accompanying symptoms and etiological development. The claims also are drawn to a composition comprising MHC molecules. The specification teaches the administration of MHC molecules to rats which have been inoculated with the AH-130 tumor cells, and estimating the number of tumor cells in the rats after the various administrations. There is no teaching in the specification that these data (drawn to the number of cells pre and post treatment) reflect the treatment of tumors. What is not clear is the survival of these rats past the treatment mode and the status of all symptoms associated with the cancer state. There are no working examples of an effective treatment of a cancer. There are a number of types of cancers that do not grow in the way exemplified - the exemplification is at best an alternate to an in vitro culture, as it serves to demonstrate a proliferation of tumor cells at a specific site (by virtue of the fact that they are specifically inoculated into the area as for e.g. Into the lungs) with the therapeutic compositions also being administered into the same site. Secondly the window of testing for the efficacy of the composition is about 18 days and the time of administration begins as early as 4 days. This is very unlike the development of cancer in a human where it is not certain when the cancer state began

or when tumor cells started forming. An effective therapeutic protocol for the treatment or prevention of the formation of a tumor is subject to a number of factors which enter the picture beyond simply the administration of MHC molecules. The establishment and growth of a tumor is subject to variables beyond simply growing in an acceptable host. The specification does not indicate what type of cells the AH-130 cells are or whether the rats were immunosuppressed. The ability of a host to suppress and thereby prevent the tumor from establishing itself will vary depending upon factors such as the condition of the host, the type of tumor (rapidly proliferating or slowly proliferating) and the tumor burden. Moreover, the examples delineating the preparation of the compositions that are administered are extracts of the liver tissue from goat or calf. Firstly, the extract is a mixture of all molecules ranging in molecular weight from "10, 000-50, 000" (presumed to be Daltons). Such a mixture could have different proteins or chemically different molecules other than the MHC molecules, that could very well have therapeutic benefits. Therefore, the claims are not enabled with respect to a pharmaceutical composition comprised of an effective amount of MHC molecules, because there is no guidance in the specification as to how to determine the amount of the MHC molecules in the extract. The facts of the experiments described are not sufficient to prove that the invention is enabled for treating cancers. Further, the disclosure does not provide working examples wherein all of the steps required to practice the method are employed. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art such as the treatment of cancer. In the instant case, the claims are so broadly drawn, the guidance is so limited, and the art is so unpredictable that skilled artisan is presented with a multitude of un-linked alternatives with no guidance as to which will enable use of the invention as claimed. Among these are (I) whether to use autologous or allogeneic MHC molecules (specification teaches xenogeneic "MHC molecules", (ii) which of many cancers to select for treatment, (iii) which of many antigens (e.g., endogenous/exogenous; cancer-associated/tumor-specific)are in the purified extract, (iv)

which of many neoplastic diseases to select, and (v) what dosage, schedule, and route of administration will provide a successful therapeutic outcome.

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

13. Papers related to this application may be submitted to Group 1642 by facsimile transmission. Papers should be faxed to Group 1642 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242 or (703) 305-3014.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Geetha P. Bansal whose telephone number is (703) 305-3955. The examiner can normally be reached on Mondays to Thursdays from 7:00am to 4:30pm and alternate Fridays from 7:00am to 3:30pm. A message may be left on the examiner's voice mail service.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Paula Hutzell, can be reached on (703) 308-4310.

15. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Geetha P. Bansal
October 22, 1998.

Toni R. Scheiner

TONI R. SCHEINER
PRIMARY EXAMINER
GROUP 1600